Selection of Human Recombinant Antibodies Against Wnt1: A Promising Strategy for Immunotherapy of Cancers with Wnt1 Overexpression

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Introduction

- Wnt family comprises 19 secreted glycoproteins. Aberrant activation of Wnt signaling pathway is implicated in a wide variety of human cancers. Inhibition of Wnt signaling pathway induces significant apoptosis in various cancer cell lines. Nowadays, Development of monoclonal antibodies in targeted therapy represents a milestone for both researchers and physicians. Advances in the identifying of critical molecular pathways for tumor growth and survival have facilitated the development of these targeted therapies in cancer treatment. Recombinant single chain fragment variable (scFv) antibodies are introduced as useful tools for cancer immunotherapy due to their human origin, small size and good penetrating properties. In this study specific scFv antibodies are selected against Wnt1 to provide a new cancer targeting strategy.

Methods

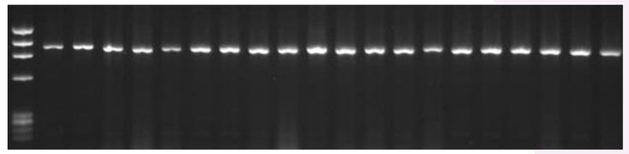
- A phage display technology was used to isolate specific anti-Wnt1 scFvs. A phage antibody display library of scFv was panned against an immunodominant epitope of Wnt1. The selected clones were amplified by PCR and DNA fingerprinted to show the common patterns. Phage ELISA was performed to test the specificity of the selected antibodies.

Discussion

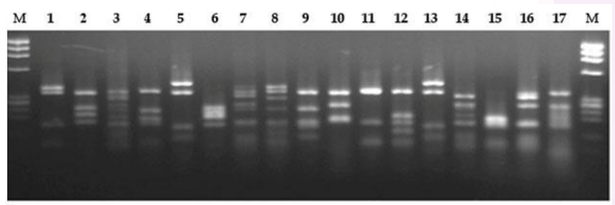
- Wnt1 signaling pathway is over expressed in many tumors including colorectal, lung , breast and head and neck cancers. In this study we successfully selected two specific scFv antibodies against Wnt1 which reacted only with the Wnt1 epitope in phage ELISA. The anti-Wnt1 characteristics such as human origin, ability to be manipulated by genetic engineering and to be conjugated with other drugs, offer their therapeutic advantages for targeted therapy of cancers with Wnt1 over-expression. Further investigations are needed to show the effects of these selected antibodies in vivo.

Results

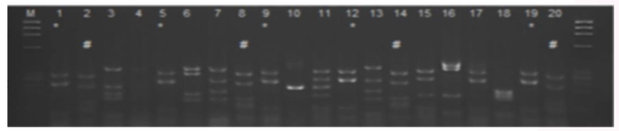
- PCR of the library clones revealed the presence of VH-linker-VL inserts.



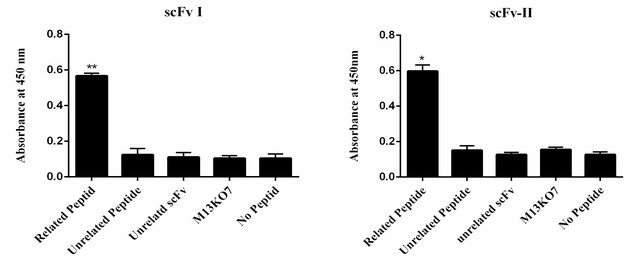
- Fingerprinting of the library demonstrated diversity and heterogenesity of the library.



- Results of fingerprinting of the selected clones after panning showed two specific single chain antibodies with frequencies of 25% and 20%.



- Phage ELISA showed the specificity of scFv1 and scFv2 against the immunodominant epitope of Wnt1.



- Reaction of specific scFvs with the related peptides were significantly higher than unrelated peptides and the antigen and antibody controls.

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